DAVINCI MEDICAL ACADEMY

SUBJECTS IN NUTSHELL FOR EFFECTIVE REVISION

PHYSIOLOGY IN NUTSHELL

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- Subthalamic nucleus [body of Luys]
- Substantia nigra

Functions:

- ✓ Planning & programming of movements.
- ✓ Regulation of sub conscious gross movements.
- ✓ Caudate nucleus- cognition.
- ✓ Globus pallidus- provides muscle tone for skilled movements.
- ✓ Substantia nigra- centre for co ordination of impulses for skilled movements.

Diseases of B. G:

- Parkinsonism – Paralysis agitans/ shaking palsy.
  - Lesion: degeneration of dopaminergic nigro striatal tract.
  - Features: rigidity, pill rolling resting tremors, Brady kinesia.
- Chorea – Caudate nuclear lesion
- Athetosis- lesion of lenticular nucleus.
- Hemi ballism- lesion of sub thalamic nucleus.
- Huntington's disease: lesion of GABAergic & Cholinergic neurons that project to the putamen.
- Wilson's disease & Kernicterus

CEREBRAL CORTEX

Lobe	Area	Location	Representation	Function	Effect of lesion
Frontal lobe	Motor area **4**	Precentral gyrus and Para central lobule	Upside down	Controls voluntary activities of the opposite half of body	Contra lateral Paralysis and jacksonian fits
	Pre motor area **6**	Posterior parts of superior, middle and inferior frontal gyri	-	Controls extra – pyramidal system	Often mixed with Pyramidal effect
	Frontal eye field **6,8**	Posterior part of middle frontal gyrus	-	Controls horizontal conjugate movements of the eyes	Horizontal conjugate movements are lost
	Motor speech area (Broca's area) **44,45**	Pars triangularis and pars opercularis	-	Controls the spoken speech	Aphasia (motor)
	Prefrontal area	The remaining large, anterior part of frontal lobe	-	Controls emotion, concentration, attention and judgment, higher intellectual functions	Loss of orientation
Parietal lobe	Sensory (somesthetic) area **3,1,2**	Post central gyrus and paracentral lobule	Upside down	Perception of exteroceptive (touch, pain and temperature) and proprioceptive impulses	Loss of appreciation of the impulses received
	Parietal area	Between sensory and visual areas		Stereognosis and sensory speech	Astereognosis and sensory aphasias
	Visuo sensory area or striate area **17**	In and around the post calcarine sulcus	Macular area has largest representa	Reception and perception of the isolated visual impressions of colour, size , Form motion, illumination	**Homonymous hemianopia with macular sparing**

Occipital lobe			tion	and transparency	
	Visuopsychic area para striate and peristriate areas **18,19**	Surround the striate area	-	Correlation of visual impulses with past memory and recognition of objects seen and also the depth	Visual agnosia
Temporal lobe	Auditosensory area **41,42**	Posterior part of superior temporal gyrus and anterior transverse temporal gyrus	-	Reception and perception of isolated auditory impressions of loudness, quality and pitch	Impaired hearing
	Audito psychic area **22**	Rest of the superior temporal gyrus	-	Correlation of auditory impressions with past memory and identification (interpretation) of the sounds heard	Auditory agnosia

Layers of typical cerebral cortex [neo cortex/ isocortex]

- **Layer: I**. Molecular/ plexiform layer
- **Layer: II**. External granular layer
- **Layer: III**. External or outer pyramidal layer
- **Layer: IV**. Internal granular layer
- **Layer: V**. Internal pyramidal layer
- **Layer: VI**. Fusiform layer
  - **Allo cortex**: < 6 layers- Uncus, hippocampus & gyrus dendatus.
  - **Neo cortex**: all 6 layers.

Brodmann area:

I. Primary motor area- precentral gyrus – Area 4
II. Premotor area- Area 6
III. Primary visual area-Area 17
IV. Visual association area- Area 18,19
V. Primary audiitory area- Area 41
VI. Auditory association area- Area 42, 22
VII. Frontal eye field- Area 8 & 6
VIII. Broca's area- Area 44
IX. Primary sensory area- postcentral gyrus -Area 3, 1 ,2
X. Somato sensory association area- area 5,7

PAPEZ CIRCUIT:

- A closed circuit formed by the pre-frontal lobe with the thalamus.
- Responsible for resting EEG & plays an important role in emotional behavior.

Anterior nucleus of thalamus----------→ **cingulate gyrus (Area-24) of pre frontal lobe**
↑ **MAMMILOTHALAMIC TRACT** ↓
Mamillary body [HT] ←----------**hippocampus**
FORNIX

EFFECTS OF LESION:

- **B/L Pre-frontal lobectomy**: marked deterioration of social behavior, inability to check emotions.
- **Pre frontal Leucotomy**: cutting the connections between thalamus & frontal lobe.
- "**Frontal lobe syndrome**"- Euphoria, impaired recent memory, flight of ideas, emotional instability, and attention deficit
- **B/L temporal lobectomy**: **Kluver-Bucy syndrome**- hyper phagia, omni phagia, visual agnosia, increased oral activity, hyper Meta morphosis- failure to explore peripheral stimuli.

Limbic system [Rhinen cephalon]

Consists of:

- **Limbic lobe**:
  - cingulate gyrus,
  - hippocampal gyrus,
  - isthmus & uncus.
- **Subcortical nuclei**:
  - Amygdala,
  - septal nuclei,
  - hypothalamus & anterior thalamic nuclei.

Functions:

- autonomic functions,
- emotions of rage,
- behavioral aspect of anger,
- olfaction & memory.
- **Genesis of emotion: Hypothalamus & Limbic system**.
- **Sham rage**:
  - ✓ seen in animals with diencephalic lesion i.e. transection of the neural axis above the thalamus.
  - ✓ Removal of neocortex, destruction of ventromedial hypothalamic nuclei or destruction of septal nuclei leads to **sham rage** (physical manifestations of rage without emotion)

Higher functions

Language: [speech]

CEREBRAL DOMINANCE	
Dominant Hemisphere	**Non – dominant Hemisphere**
○ Also called categorical hemisphere	○ Also called representation hemisphere
Functions: ✓ Understanding & Expression of speech and ideas. ✓ Categorization ✓ Symbolization	**Functions:** ✓ Spatio – temporal relations ✓ Identification of form of objects ✓ Recognition of faces ✓ Recognition of musical themes
Lesions: Language disorders	**Lesions:** • Astereognosis, Agnosia

- **Salient Points:**
  - Lesions producing agnosia & astereognosis are generally in parietal lobe. If the inferior parietal lobule is involved unilateral neglect & inattention occurs.

HANDEDENESS

- In 96% of right handed persons, dominant hemisphere is the left. But, only 15% of left handed persons have dominant right hemisphere.
- 70% of left handers have dominant left hemisphere.
- Dyslexia: 12 times more common is left handers.
- Left handers have slightly shorter life span than right handers.

Sensory speech centres:

- **Spoken speech**: INTACT AUDITORY PATHWAY: **Wernicke's area** [area-22], located in the posterior end of the superior temporal gyrus in the dominant hemisphere. It is concerned with comprehension- interpretation & understanding of auditory and visual impulses.
- **Written speech**: INTACT VISUAL PATHWAY: **Dejerine area** [area-39], located in the angular gyrus in the dominant hemisphere behind Wernicke's area.
- **Motor speech areas:**
  - **Broca's area**: Area-44, located in the inferior frontal gyrus of the dominant hemisphere.
  - **Exner's area**: motor writing area, located in the middle frontal gyrus of the dominant hemisphere.

Speech disorders:

- **Aphasia**-abnormalities of language functions that is not due to defects of vision or hearing or motor paralysis.
- Sensory/ fluent aphasia: lesion of **Wernicke's area**
- Motor/ non fluent aphasia: lesion of **Broca's area.**
- Pure word blindness [alexia], anomic aphasia: **Dejerine area**
- Global aphasia: lesion of both **Wernicke's & Broca's area**

	Motor/ non fluent aphasia	Sensory/ fluent aphasia
Site of lesion	• Inferior frontal gyrus	• superior temporal gyrus
Cause	• Occlusion of superior branch of MCA.	• Occlusion of inferior branch of MCA
Comprehension	• Intact except for grammar	
Fluency	• Decreased	• Preserved / increased. Jargon's neologism
Naming	• Impaired	• Impaired
Repetition	• Impaired	• Impaired
Neologism	• Absent	• Present
Insight	• Preserved	• Not preserved

Learning

- Ability to alter the behavior on the basis of experience.
- **Classical conditioning**:
  - Based on reflexes: inborn or unconditioned reflexes, conditioned reflex.
  - Described by Pavlov in 1927.
- **Operant conditioning**:
  - Developed by Skinner
  - based on his experiments, he formulated the presence of reward centres and punishment areas in the limbic system.
- **Mechanisms implicated in learning**:
  - Sensitization
  - Habituation
  - Association
  - Positive reinforcement

Memory

- Ability to recall the past events at the conscious or unconscious level.
- **Declarative or Explicit memory**: involves conscious recall of events.
- **Types**:
  - ✓ Recent/ short term memory- Hippocampus
  - ✓ Working memory- Prefrontal lobes
  - ✓ Remote/ long term memory - Neo cort
  - ✓ **Non-declarative or Implicit or reflexive memory**: largely unconscious & involves skills, habits, classical conditioning etc…
- **Mechanisms implicated in memory**:
  - ✓ Post tetanic potentiation
  - ✓ Long term potentiation
  - ✓ Changes in synaptic strength
  - ✓ Increase in synaptic contacts
- **Mechanisms implicated in learning & memory:** Synaptic plasticity
- **Alzheimer's disease**:
  - **Pathogenesis:** Aggregation of β amyloid plaques→ formation of extra cellular plaques→ inflammatory reaction with oxidative damage → altered nerve fibres & glial damage → formation of intra cellular neuro fibrillary tangles → degeneration of cholinergic neurons in the cerebral cortex & hippocampus→ Alzheimer's disease.

Motivation and addiction

- Forebrain neurons in the ventral tegmental area and nucleus accumbens are involved in motivated behaviors like reward, laughter, pleasure, addiction and fear.
- The mesocortical dopaminergic neurons that project from the midbrain to the nucleus accumbens and the frontal cortex are also involved in motivation.
- Alcohol & addiction are associated with the reward system.

- The different drugs like opiates, cocaine, amphetamines and cannabinoids affect the brain in different ways, but all of them increase the amount of dopamine available to act on **D_3 receptors** in the nucleus accumbens.
- These drugs stimulate the reward centres on acute use, but long term addiction involves the development of tolerance.

Vestibular apparatus [labyrinth]

Consists of:

- 3 semi circular canals
  - Horizontal / lateral
  - Superior / anterior
  - Inferior / posterior
- Otolith organs, saccule & utricle.

Functions:

- **Otolith organs-** Linear acceleration.
- **Saccule**- vertical acceleration.
- **Utricle**- horizontal acceleration.
- **Semi circular canals-** Angular acceleration
- Used in the regulation of equilibrium & orientation in space.

Effects of labyrinthectomy:

- **Unilateral labyrinthectomy**:
  - ✓ Immediate- Nystagmus, head (Occiput) is turned to the side of lesion, flexion of I/L limbs and extension of C/L limbs.
  - ✓ Permanent – Nystagmus, decreased rotation of the trunk
- **Bilateral labyrinthectomy**:
  - ✓ behaves normally with intact vision.
  - ✓ cannot right himself when blinded.
  - ✓ Transient loss of muscle tone.

Endolymph	Perilymph
• Fills the Scala media, Utricle, Saccule and the three semicircular canals.	• Fills the Scala tympani, Scala vestibule, the vestibule and the periotic space of semicircular canals
• Absorbed by the endolymphatic sac and finally drains into dural venous sinuses.	• Communicates with CSF in sub arachnoid space surrounding the brain via Perilymphatic duct.
• Has high K^+ Content and low Na^+(ECF that resembles ICF) .	• High concentration of Na^+ and low K^+(resembles ECF & CSF).

CHEMICAL TRANSMITTERS OF CNS

- The transmitters are of two types:
  - Small & rapidly acting: Ach, amines (EN, NE and Dopamine) & AA's (glycine & GABA).
  - Large & slowly acting: opioids, GIT hormones, ATP, substance-P and neuropeptide-Y.

Acetylcholine:

- It is excitatory transmitter present in spinal cord, basal ganglia and cortex.
- It acts on M_1receptor and essential for the intellectual functions as memory, arousal state and motor function.
- Deficiency in cortex leads to Alzheimer's D.

Epinephrine and nor epinephrine:

- They are excitatory & present in brain stem and hypothalamus.
- They are important for improving the mood and preventing fatigue.
- Deficiency leads to behavior changes as in schizophrenia.

Dopamine:

- It is an inhibitory transmitter present in basal ganglia, hypothalamus and limbic system.
- Its deficiency in basal ganglia leads to Parkinsonism.
- In hypothalamus, it acts as a Prolactin inhibitory factor.

Serotonin:

- It is present in hypothalamus and brainstem mainly raphe nucleus.
- It stimulates Prolactin release, reduce food intake, blocks pain conduction, and induce sleep.

Gama-amino-butyric acid:

- Acts as a presynaptic inhibitor & needs pyridoxine (Vit.B6) for its synthesis.
- Deficiency of the vitamin decreases the formation of GABA and leads to convulsions.

Glycine

- Acts as a postsynaptic inhibitor. It activates Cl^-channels and increases Cl^- influx.

Glutamate and aspartate:

- Glutamate constitutes about 75% of the excitatory transmitters in brain.
- It is essential for memory and learning. Excess glutamate induces neuronal damage.

BLOOD BRAIN BARRIER

Formed by: • Tight junctions of endothelial cells. • Foot process of astrocytes.	○ Allows only lipid soluble substances. ○ Allows: ○ Carbon dioxide, oxygen, water, bile salts & glucose.	**Area outside BBB:[Circum-Ventricular organs]:** • Median eminence of hypothalamus. • Sub fornical organ • Organum Vasculosum of Lamina Terminalis (OVLT) • Area Prostrema. • Posterior pituitary

- **Salient Points:**
  - ✓ Dopamine can't cross BBB, but L – dopa can.
  - ✓ Bile salts can cross BBB, but bile pigments can't.
  - ✓ GLUT- 1 is the major glucose transporter across BBB

CEREBROSPINAL FLUID

Formation:

- 50-70% in Choroid Plexus
- Remaining: Blood Vessel
- Ventricular walls
- Cell- <5 lymphocytes/mm^3

○ **Salient Points:**

- ✓ Volume→ 150ml
- ✓ Rate of CSF turnover: 3 times /day or Rate of CSF formation: 550ml/day
- ✓ PH: 7.33

Characters:

- Appearance – Colorless, clear
- Sugar – 2/3rd of plasma – 40-70 mg/dl
- Proteins – 20-40mg/dl

- ✓ Pressure: 10mmHg/130mm of H_2O (on Lying Posture) Range: 50-180mm of H_2O
- ✓ All positive ions are more in Plasma than CSF **except Mg^{2+}**
- ✓ All negative ions are more in CSF.

○ **Clinical aspects**:

- Decorticate animal- removal of cerebral cortex, intact sub cortical structures.
- Decerebrate animal- transection of the connections at the superior border of Pons.
- Midbrain preparation- transection of the neural axis on top of the midbrain.
- Spinal preparation- spinal cord transection at mid thoracic level.

○ **Cerebral blood flow: 750 ml/min (15% of cardiac output).**

○ **Oxygen consumption: 3.5 ml/ 100g/ min**

SPECIAL SENSES
VISION

- **Layers of the retina**:

Layer	Feature
I-Pigmented Epithelium	• Contains melanin & choroidal pigment & prevents reflection of light
II- Rods & Cones	• Photo receptors
III-External limiting membrane	
IV- Outer nuclear layer	• Nucleus of rods & cones
V- Outer Synaptic layer	• Synapse between rods & cones + dendrites of bipolar cells & horizontal cell processes.
VI-Inner nuclear layer	• Bipolar cells, Horizontal® cells & Amacrine* cells
VII-Inner synaptic layer	• Synapse between axons of bipolar cells + dendrites of ganglion cells. • **Major site of processing of visual image.**
VIII-Ganglion cell layer	• Single layer of cell containing round cells
IX-Optic nerve	• Formed by joining the axons of ganglion cells
X-Internal limiting membrane	• Separates the retina from the vitreous humour

- **Horizontal cells**- connect the receptor cells to one another.
- **Amacrine cells**- connects dendrites of ganglion cells & bipolar cells, connects ganglion cells to one another.
  - The neural elements of the retina are bound together by glial cells called Muller cells. The processes of these cells form an internal limiting membrane on the inner surface of the retina and an external limiting membrane in the receptor layer

Electrical responses in the eye:

- Receptor potentials of the photo receptors and other neural elements in the retina are local, graded potentials and it is **only in the ganglion cells that all or none action potentials are generated**.
- Reponses of different cells on stimulation:
  - Rods, cones, horizontal cells- hyperpolarisation
  - Bipolar cells- hyper polarization/ depolarization
  - Amacrine cells- depolarizing potentials & spikes that may act as generator potentials.
- **Cone receptor**:
  - → Potential has a sharp onset & a sharp fall.
  - → Cone responses are proportionate to stimulus intensity at high levels of illumination when the rod responses are maximal& cannot change.
  - → Cones generate good responses to changes in light intensity above back ground but do not represent absolute illumination.
- **Rod receptor:**
  - → Potential has a sharp onset but a slow fall.
  - → Rod responses are proportionate to stimulus intensity at levels of illumination that are below the threshold for cones.
  - → Rods detect absolute illumination.

VISUAL PATHWAYS

- **Origin**: Visual fibres arise in the layer of nerve cells (bipolar & ganglion cells)
- **First order neurons**: bipolar cells [dendrites- synapse with photo receptors, axons- synapse with dendrites of ganglion cells]
- **Second order neurons**: ganglion cells. [Ganglion cells→ Optic nerve→ optic chiasma→ optic tract→ LGB & Superior Colliculus]
- **LGB**: contains orderly topographical representation of the cornea.
  - Grey matter shows six layers numbered 1-6.
  - Fibres from opposite retina terminate in layers 1, 4 and 6.

- Fibres from ipsilateral retina terminate in layers 2, 3 and 5.
- Fibres from upper retinal quadrant terminates in medial halves of LGB while from lower quadrants terminate in lateral halves.

- **Third order neurons**: neurons located in the LGB [geniculo- Calcarine tract]

Visual Cortex:

- Made of 6 layers:
- Axons from LGB neurons→ end n pyramidal cells of layer 4 → layer 2 & 3.
- These layers contain cluster of cells called **blobs**, responsible for colour vision.

Primary Visual area/ Visuo sensory area (Area 17):

- Located in the medial surface of occipital lobe, above & below the Calcarine fissure.
- Upper retinal quadrant → medial halves of LGB→ superior lip of Calcarine fissure.
- Lower retinal quadrant → lateral halves of LGB→ inferior lip of Calcarine fissure.

ORGANIZATION AND FUNCTION OF VISUAL PATHWAYS		
Ganglion cells	✓ M (or Y) cells	✓ P (or X) cells
Lateral Geniculate Body	✓ Large cell layers 1 & 2	✓ Small cell layers 3,4,5,6
Pathway	✓ **Magno cellular**	✓ **Parvo cellular**
Visual cortex	✓ Superficial layer 4	✓ Deep layer 4
Functions	✓ Detection of movement, depth & flicker	✓ Detection of colour, shape & fine details

- Fibres of macular vision- end posteriorly on the lips of Calcarine fissure. (Very large central representation).
- 1mm of fovea in the retina – 16mm in the cortex.
- Peripheries of the retina- 1/60th of mm.
- Concerned with **colour vision & visual discrimination**.

Visual association areas/ Visuo psychic area (Area 18):

- above & anterior to area 17.
- Concerned with visual orientation & depth perception.

Occipital eye field (Area 19):

- lateral surface of occipital lobe. Concerned with deviation and movements of eyeball.

PHYSIOLOGY OF VISION

Reduced eye: [Schematic eye]

- Power: 59D.
- Nodal point: 7 mm behind the anterior surface of retina.

Visual reflexes:

- **Light reflexes:**
  - Light→ optic nerve→optic tract→superior colliculi/ pretectal nucleus→ III nerve (Edinger-Westphal nucleus)→ Ciliary ganglion → short ciliary nerve→ sphincter pupillae.
- **Accommodation reflex:**
  - Visual information→ visual pathway→ area 17→ area 8→ III nerve (Edinger-Westphal nucleus)→ Ciliary ganglion muscle, medial rectus &sphincter pupillae.

PHOTO CHEMISTRY OF VISION

A. PHOTOPIC & SCOTOPIC VISION:

- **Photopic** – day light- cones [higher threshold: 1mA]
- **Scotopic**- dim light- rods [minimal threshold: 0.001mA]
- **Mesopic** – full moon light vision, 0.01mA

- Existence of rods & cones- Duplicity theory.
- Photoreceptors: RODS AND CONES

○ **Outer segment:**
- Modified cilia, made of discs or saccules.
- Discs or saccules contain rhodopsin (rods) & Iodopsin (cones)

○ **Inner segment:**
- Rich in mitochondria & it pierces the external limiting membrane.
- Has the Na^+ K^+ ATPase which maintains the equilibrium.
- In peripheral retina→ rods predominate.
- Per eye:
  - ✓ Cones- 6-7 million
  - ✓ Placed outermost towards the choroid.
  - ✓ Both made of two segments- outer & inner.
  - ✓ Rods- 120-125 million
  - ✓ Optic fibres in each optic nerve: 0.8-1.2 million.
- **Convergence of receptors** through bipolar cells on ganglion cells in the ratio of 105-165: 1

B. VISIBILITY OR SENSITIVITY CURVE:
○ Visible or sensitive range of vision : 400nm-750nm.
○ **Purkinje shift/phenomenon**:
- Shifting of photopic vision to scotopic vision, mainly in the evenings.

C. PHOTOSENSITIVE PIGMENTS:
○ **Rhodopsin**[rod pigment/ visual purple]:
- Contains scotopsin + $retinene_1$- aldehyde of Vit-A.

Visual cycle:

○ **Iodopsin**[cone pigment]:
- Maximum sensitive to 560nm- greenish yellow.
- Contains opsin + $retinene_1$
- Iodopsin→ on exposure to light → opsin + $retinene_1$

ELECTROPHYSIOLOGY OF VISION

- RMP of rods and cones: -40mv.
- Response to light: hyperpolarisation (not depolarisation)
- Light decreases the concentration of both Na & Ca inside the photo receptors → activation of guanylate cyclase→ more cGMP→ opens Na channels.

Theories of colour vision:
- Helmhotz theory: The basis of 3 primary colours is the existence of three types of cone receptors (red, green, blue)

HEARING

Velocity of Sound
- More in salt water: Salt water > Fresh water (1450m/sec) > Air (344m/sec)
- Unit of amplitude: Decibel
- Unit of frequency: Hertz (cycles per unit time)
  - ✓ **Audible frequency:** 20HZ – 20,000 HZ i.e., 20HZ – 20 kHz
  - ✓ **Greatest Sensitivity of hearing:** 1000 – 4000 HZ
  - ✓ Pitch of average male voice: 120HZ; Pitch of average female Voice: 250HZ

○ **Receptors for hearing**: organ of corti.- made of inner & outer hair cells.

	Inner hair cells	Outer hair cells
Arrangement	• Single row	• 3or4 rows
Population	• 3500 per cochlea	• 20000 per cochlea
Support	• Phalangeal cells	• Deiter's cells

Innervations	• Dense	• Sparse
Function	• Primary sensory cells for hearing, fine auditory discrimination	• Improvement & helping in hearing

Impedance matching:

- The lever system of middle ear ossicles magnifies the sound intensity **1.3 times.**
- Reduction of area from Tympanic memb (50sq.mm) to oval window (3mm)→ **17 times.**
- **Both increases the intensity of the incoming sound to 22 times (Impedance matching).**

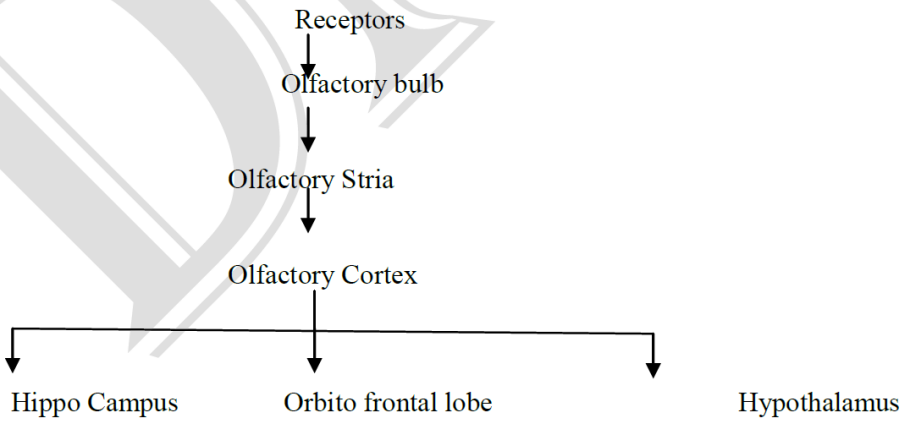
Tympanic reflex:

- Protective reflex against loud sound.
- Contraction of the tensor tympani & stapedius→ prevents loud sounds from entering the inner ear.
- Reaction time 40-160msec.

HEARING PATHWAY

Organ of Corti
↓
Bipolar cells of Spiral ganglion
↓
Cochlear nuclei
↓
Superior Olivary nuclei
↓
Lateral lemniscus → Inferior Colliculus (centre for auditory reflexes)
↑
Medial Geniculate body
↑
Primary auditory Cortex(area – 41)
↑
Other auditory areas (42, 22)

SMELL PATHWAY



- Each olfactory receptor is a neuron.
- They have short, thick dendrites with expanded ends called olfactory rods.
- The axons of the olfactory receptor neurons pierce the cribriform plate of the ethmoid bone.

TASTE PATHWAY

Taste modality	Location of receptors in the tongue	Mechanism of action
Sweet	• Tip of tongue	• H^+ ions

Salt	• Tip of tongue	• Na^+ ions
Sour	• Sides of tongue	• Cations
Bitter	• Back of tongue	• Organic acids
Umami	• A variant of sweetness	

- The sodium channel blocker amiloride blocks the sodium channels and masks the salt sensations.

Taste buds

↓

Tractus Solitarius

↓

Nucleus Tractus Solitarius (NTS)

↓

Postero medial (VPM) nucleus of thalamus

↓

Infero lateral part of Post Central gyrus (43)

- **Some IInd order fibres in the medulla reach salivary nucleus, Vomiting centre, limbic System ,dorsal nucleus of Vagus and hypothalamus**

LEPTIN

✓ Polypeptide, produced by adipose tissue
  ✓ **MECHANISM**: ↑ed adiposity of the body→↑ed leptin production→Enters blood→Reaches hypothalamus→Binds to Hypothalamic leptin receptors→Decreases food intake

- **Human obesity may be due to lack of leptin receptors.**
- **Leptin causes Suppression of Neuropeptide – Y Synthesis.**

OREXINS

- Brains from humans with narcoplexy often contain fewer **hypocretin (orexin)** producing neurons in the hypothalamus.

CARDIO VASCULAR SYSTEM AND CIRCULATING BODY FLUIDS

CIRCULATORY OF THE CARDIOVASCULAR SYSTEM

- Cardiac output from the left side of heart- systemic blood flow.
- Cardiac output from the right side of the heart - pulmonary blood flow.

HEMODYNAMICS

- **Arteries**
  - deliver oxygenated blood to the tissues. thick-walled
  - extensive elastic tissue and smooth muscle.under hig h pressure.
  - blood volume contained in the arteries
  - called the stressed volume.
- **Arterioles**
  - smallest branches of the arteries.
  - site of highest resistance in thecardiovascular system .
  - have a smooth muscle wall
  - extensively innervated by autonomic nerve fibers. arteriolar resistance is regulated by the ANS-

    1. Adrenergic receptors
    - **skin, splanchnic**, and **renal** circulations.

    2. Adrenergic receptors
    - found on arterioles of **skeletal muscle.**
- **Capillaries**
  - have largest total cross-sectional and surface
  - consist of single layer of endothelial cells surrounded by basal lamina.
  - are thin-walled.
  - are the site exchange of nutrients, water, and gases.
- **Venules** -are formed from merged capillaries
- **Veins**
  - progressively merge to from larger veins
  - are thin-walled
  - are under low pressure.
  - contain the **highest proportion of the blood** in the cardiovascular system
  - blood volume contained in the veins called the **unst ressed volume** -have α1 adrenergic receptors

Velocity of blood flow

- can be expressed by the following equationv=Q/A
- where
  - V= velocity (cm/sec)
  - Q= blood flow (ml/min)
  - A= cross-sectional area (cm^2)
- At any level of the cardiovascular system velocity is
  - ✓ **directly proportional** to blood flow
  - ✓ **inversely proportional** to the cross-sectional area

Blood flow

- can be expressed by the following equation:
  - ✓ Q = P gradient/R

- Q=flow or cardiac output (m/min)
- P = pressure gradient (mm Hg)
- R = resistance or total peripheral resistance (mm Hg/ml/min)

- Blood flow is inversely proportional to the resistance of the blood vessels.

Resistance

- poiseuille's equation gives factors that changes the resistance of blood vessels.
- $R = 8nl/pi\ r^4$
  - Where:
    - ✓ R= Resistance
    - ✓ V= viscosity of blood

- ✓ L= Length of blood vessel
- ✓ r^4= radius of blood vessel to the fourth power

- Resistance is directly proportional to the **viscosity of the blood**

CONDUCTING SYSTEM OF THE HEART:

Anatomy:

- **S.A.Node**: situated at the junction of Superior Vena Cava with Right atrium. Pace maker [P] cells are seen here which discharge impulses more rapidly than any other tissue.
- **A.V.Node**: located posteriorly on the right side of the interatrial septum near the opening of coronary sinus. It is the only conducting pathway between the atria & ventricles.
- There are three bundles of atrial fibres that contain purkinje type fibres and connect the S.A.Node to the A.V. node. These inter nodal tracts are:
  - **Anterior -Bachman.**
  - **Middle -Wenckebach.**
  - **Posterior -Thorel**
- Conduction also occurs through atrial myocytes, but it will be very slow than the conduction in these bundles.
- **Bundle of His**: Right bundle branch + left bundle branch [anterior & posterior fascicles]

Blood supply:

- SA Node: atrial branches of Right Coronary artery (65%), Left coronary artery in 35%.
- AV Node & Bundle of His: Right Coronary artery
- RBB: Left coronary artery
- LBB: Left coronary artery (mostly)/ Right Coronary artery

Nerve supply:

- S.A.Node: Right vagus & Right sympathetics
- A.V. Node: Left vagus & left sympathetics.

Properties of cardiac muscle

A. Excitability:

- RMP of myocardial fibers= -90mV.
- **Phases of action potential**
- **Depolarization**
  - ✓ **Phase-0**: rapid depolarization and potential reaches +20mV -30mV. Due to Na^+ influx via rapidly opening Na channels.
- **Repolarisation**
  - ✓ **Phase-1**: Rapid initial fall from +30mV to -10mV due to inactivation of Na^+ channels.
  - ✓ **Phase-2**: A plateau phase in which the membrane potential slowly falls to -40mV due to Ca^{2+} influx.
  - ✓ **Phase-3**: rapid fall in membrane potential to the resting value of -90mV due to K^+ efflux.
  - ✓ **Phase-4**: polarized state.

B. Autorhythmicity:

- The heart continues to beat for sometime even after all the nerves are sectioned. This is due to the presence of the specialized pacemaker tissue in the heart.
- The pace maker tissue is characterized by an unstable RMP because of continuous change in membrane permeability. This slow depolarization between action potentials is called pre-potential or pace maker potential or diastolic depolarization.

Parts of pre-potential (PACE MAKER POTENTIAL):

- **Depolarization**: once membrane potential reaches -40mV, there occurs rapid depolarization due to
  - Increase in long lasting Ca^{2+} influx. (**mainly**)

- Increase in Na^+ influx.

- **Repolarisation:** starts with K^+ efflux.

Tissue	Rate of impulse generation
S.A. Node	70-80/min
A.V. Node	40-60/min
Bundle of His	40/min
Purkinje fibres	24/min

- Last part of the heart to be depolarized:
  - ✓ Postero basal portion of left ventricle.
  - ✓ Pulmonary conus
  - ✓ Upper most portion of the septum.

	Depolarization	Repolarisation
Single ventricular muscle fiber	• From endocardium to epicardium	• From endocardium to epicardium
Whole heart	• From endocardium to epicardium	• **From epicardium to endocardium**

C. Contractility:

- Depends on **Frank starling law:**
- Energy of contraction is directly proportional to initial length of cardiac muscle fibre.

D. Conductivity:

- Conduction rate in decreasing order **(m/s):**
- **Purkinje fibres > [bundle of His = Ventricular muscle = Atrial pathways] > [SAN = A.V. Node]**
  (4m/s) (1m/s) (1m/s) (1m/s) (0.05m/s) (0.05m/s)
- Conduction also occurs through atrial myocytes, but it will be very slow than the conduction in these bundles.

CARDIAC CYCLE

- **DURATION: 0.8 sec.**

	Ventricle	Atrium
Systole	✓ 0.27sec	✓ 0.1 sec
Diastole	✓ 0.53 sec	✓ 0.6sec

- At the beginning of cardiac cycle, characteristic features during diastole are:
  - All the 4 chambers are relaxed and filled with blood due to venous return.
  - As A-V valve opens, atrium and ventricle of each side comes in continuity to each other and the pressure in each cavity is equal.

Phases:

1. ATRIAL SYSTOLE: ATRIAL CONTRACTION PHASE (0.1SEC)

- Follows impulse generation in the S.A. Node.
- Atrial muscle contracts and the pressure increases.
- Propels 30% of additional blood into the ventricles.

2. VENTRICULAR SYSTOLE: (0.27 SEC)

a. **Isometric contraction** : 0.05sec

- Ventricles contract and the pressure exceeds the atrial pressure.
- Closure of AV Valves→ first heart sound.
- Bulging of AV valves into the atrium.

b. **Ventricular systole proper**: (0.25 sec)- pressure in ventricles exceeds the arterial system.

i. **Rapid ejection phase**: (0.1sec)

- Intra ventricular pressure rises to the maximum and increases the ventricular output.
- $2/3^{rd}$ of the stroke volume is ejected.

- AV valves come back to original position & a sharp fall in atrial pressure occurs.

ii. **Slow ejection phase** (0.15sec)

- Ventricular contraction subsides and the pressure decreases.
  - End diastolic volume: volume of blood in the ventricles at the end of diastole. {Maximum volume of blood}
  - Stroke volume: volume of blood ejected by the ventricles per stroke at rest.
  - End systolic volume: EDV-SV.

3. VENTRICULAR DIASTOLE: (0.5SEC)

a. **Proto diastole**: (0.04sec)
- ✓ Ventricular pressure drops more rapidly. Closure of Semilunar valves→ second heart sound.

b. **Isometric relaxation**: (0.08sec)
- ✓ Initial part of ventricular diastole.
- ✓ Intra ventricular pressure drops, ventricular muscle continues to relax without change in the ventricular volume.

c. **Ventricular diastole proper:** Passive filling of ventricles (70%)
- ✓ **Initial rapid filling phase**: opening of AV Valves and continued relaxation of ventricles.
- ✓ **Slow filling phase (Diastasis):** continuous venous return filling both atrium & ventricles.

4. ATRIAL DIASTOLE: (0.7 SEC)

- Atrial muscle relaxes and the pressure gradually increases due to venous return.

- **Iso volumetric contraction phase (0.05sec):**
  - ✓ Mitral & Tricuspid valve closes→ isometric contraction→ pressure increases more than the aorta→ aorta & pulmonary valve opens.
- **Iso volumetric relaxation phase (0.08sec):**
- ✓ Aortic & pulmonary valve closes→ isometric relaxation→ pressure in the ventricles decreases than the aorta→ tricuspid & mitral valve opens.

Valvular events	Cardiac events	ECG	JVP
Opening of AV valve	• End of isometric relaxation phase	• End of T wave	• V-Y descent
Closure of AV valve	• End of diastole	• Later half of R wave	• End of x descent
Opening of semilunar Valve	• End of isometric contraction	• ST segment	• Peak of C wave.
Closure of Semilunar valve	• Beginning of diastole	• Later half of T wave	•

	Diastole	Systole
Right Atrium	• 0	• 5 mm Hg
Right Ventricle	• 0-5 mm Hg	• 15-30 mm Hg
Pulmonary Artery	• 10 mm Hg	• 15-30 mm Hg
Left Atrium	• 4 mm Hg	• 12 mm Hg
Left Ventricle	• 4-12 mm Hg	• 90-140 mm Hg
Aorta	• 60-90 mm Hg	• 90-140 mm Hg

Factors effecting stroke volume:

- **Preload** – amount ventricles are stretched by contained blood (**Venous return**)
- **Contractility** – cardiac cell contractile force due to factors other than EDV
- **After load** – back pressure exerted by blood in the large arteries leaving the heart (**blood pressure**)
  - **Cardiac index=** cardiac output/ body surface area = 3.2L/min.

- **Stroke volume=** amount of blood pumped out by each ventricle per beat = cardiac output/ heart rate = 70 ml
- Cardiac output: output of the heart per unit time = 5L/min

Methods of measuring cardiac output

Direct method	Indirect method
• Cardio meter • Flow meter	• Fick's principle • Indicator dilution principle • Thermo dilution technique • Doppler echo cardiogram

- **Fick's principle**: **Cardiac output** =O_2 consumption ml/min / Arterio -Venous O_2 difference

Factors affecting cardiac output

Increase in CO	Decrease in CO	No change
• Anxiety • Eating • Exercise • Hyperthermia • Pregnancy • Epinephrine	• Rapid cardiac arrhythmias • Heart disease • Sitting/ standing from lying posture	• Sleep • Moderate change in environmental temperature

Heart sounds

First Heart Sound	Second Heart Sound	Third Heart Sound	Fourth Heart Sound
○ Produced by closure of AV valves	○ Produced by closure of Semilunar valves	○ Produced by vibration of the ventricle & turbulence of blood flow	○ Produced by atrial systole
○ Marks the onset of ventricular systole	○ Marks the onset of ventricular diastole (end of vent. systole)	○ 1st rapid filling phase of ventricle	○ 2nd rapid filling phase of ventricle
○ *Continuous sound ○ *Lasts 0.14 – 0.17sec ○ *Audible better at tricuspid & Mitral areas ○ *Coincides with 'R'wave of ECG ○ *Dull, Prolonged, Soft, low pitched sound (LUB)	○ *Split Sound ○ *Last 0.1 to 0.14sec ○ *Audible better at Aortic and Pulmonary areas ○ *Coincides with end of 'T'wave of ECG ○ *Short,Sharp,high – pitched sound (DUB)	○ *Low Pitched Sound ○ *Lasts < 0.1sec ○ ***Audible In** ○ -30% of normal population ○ -MI ○ -Heart failure ○ Cardiomyopathy ○ -Ventricular hypertrophy	○ *Also called atrial sound ○ *Low – pitched Sound ○ **Audible in** ○ -MI ○ -Heart failure

- **Gallop Triple Rhythm:S_1 + S_2 with (S_3 or S_4)**

CARDIAC ARRHYTHMIAS

Disorders associated with site and rate of production of Impulse	Disorders associated with conduction defects
○ **S.A.Node:** Sinus Bradycardia, sinus tachycardia, sinus arrhythmia, sick sinus syndrome (SSS)	○ **Sino – Atrial Block**
○ **Atrium**: Atrial ectopic, atrial tachycardia, atrial flutter, atrial	○ **Paroxysmal Atrial Tachycardia** ✓ WPW Syndrome, Lown – Ganong – Lewine

fibrillation	Syndrome
○ **A.V.Node**: Nodal ectopic, ventricular tachycardia and ventricular fibrillation	**Atrio Ventricular (AV) Block** **Partial AV Block** 1. Primary Heart block 2. Secondary Heart block (Mobitz type I & II) 3. 2:1 or 3:1 block **Complete block** eg.Stokes Adams Synd ○ **Bundle Branch Block**: (Right/Left/Trans fascicular)

ELECTRO CARDIOGRAM

- Einthoven's law: lead II= lead I + lead III.
- Kirchoff's law: lead I + lead II + lead III= 0

Events in ECG:

Intervals	Normal duration in secs		Events in the heart
	Average	range	
PR interval	• 0.18	• 0.12-0.20	• Atrial depolarization & conduction through AV node
QRS interval	• 0.08	• 0.08-0.10	• Ventricular depolarization & atrial repolarisation
QT interval	• 0.40	• 0.40-0.43	• Ventricular depolarization & ventricular repolarisation
ST interval	• 0.32		• Ventricular repolarisation
P wave			• Atrial depolarization

PRINCIPLES OF CIRCULATION

- **Layers of blood vessels:**
- **3 layers:**
  - Intima – Innermost – Single layer endothelium
  - Media – Middle – Thickest layer – made of Elastic fibres & Smooth muscles
  - Adventitia – Outermost – made of elastic lamina & Collagen

ARTERIES	CAPILLARIES	VEINS
i) **Large Elastic Arteries**: • ***Windkessel Vessels Eg**. Aorta & its main branches • *Smooth muscles arranged Spirally • *More elastic • ii) **Large muscular Arteries** • *Smooth muscle content is high • *Few elastic fibres are present iii) **Smaller arteries** • *More Smooth muscle, less elastic fibres iv) **Arterioles** • *Seat of maximum Peripheral resistance • *lacks elastic fibres • *rich in smooth muscle – arranged in circular fashion	• *Smallest vessels **(exchange Vessels)** • *True Capillaries are branches from meta – arterioles, being **guarded by Precapillary Sphincter** • *True Capillaries joins to form Venules • *Capillaries are made of single layer of endothelium • *Modified smooth muscles **(Pericytes) are present**	i) **Large Veins** • *Thin walled • *Large than largest arteries • *Elastin Content is less • *Capacitance Vessels (hold maximum blood) ii) **Smaller Veins**: thin – walled iii)**Venules** • *Thin – walled but larger than arterioles • *less elastin content than arterioles

DISTRIBUTION OF BLOOD VOLUME (100%):

- Heart → 7%
- Veins → 64%
- Arteries → 15%
- Capillaries → 5%
- Pulmonary vessels→ 9%

BLOOD VESSELS

- Maximum cross sectional area: capillaries (4500)cm^2
- Minimum cross sectional area:-aorta (4.5)cm^2
- Maximum blood is contained in:-venous system (54%)
- Maximum velocity of blood:-proximal aorta (40 cm/sec), all over the aorta – mean:22 cm/sec
- Minimum velocity of blood:-capillaries
- Seat of peripheral vascular resistance:-arterioles (resistance vessels)
- Capacitance vessels (more compliance):-veins
- Windkessel vessels – aorta and large arteries
- Percentage of blood in aorta – 2%, -arteriole – 1%
- Arterioles – stopcocks of circulation

ORDER OF VELOCITY OF BLOOD	ORDER OF CROSS – SECTIONAL AREA
• Aorta >Vena Cava>Artery> Arteriole> Capillary (**min**)	• Capillaries (**max**)>Arteriole > Artery > Vena cava > Aorta

Cardio vascular regulatory mechanisms

- Auto regulation by the tissues their blood vessels which possess basal myogenic tone (BMT).
- Pace makers cells in the smooth muscles of blood vessels which increases with stretch(myogenic theory)
- **Factors affecting basal myogenic tone (BMT):**
  - **Local vasoconstriction**: due to locally released metabolites (**metabolic theory**)
    - decreased arterial pO_2
    - decreased blood pH
    - increased arterial pCO_2
    - increased osmolality l.
    - hyperthermia
    - lactic acid, K^+
    - adenosine
- **Local vasodilatation**: Serotonin, Hypothermia.

Endothelins: [I, II, III]

- ET-1: most potent vasoconstrictor.
- **Actions**:
  - CVS: increases smooth muscle contraction & HR
  - CNS: increases transport across BBB.
  - Kidney: decreases GFR, RBF & regulates Na^+ reabsorption.
  - Endocrines: increases plasma rennin, aldosterone, ANP
  - Lungs: bronchoconstrictor

Factors effecting the arteriolar calibre		
	Vaso constriction	**Vaso dilatation**
Local factors	• Hypothermia • Auto regulation	• Increased K^+, adenosine, CO_2, • Decreased O_2, • Decreased local pH • Increased local temperature
Endothelin products	• ET-1 • Serotonin • TxA-2	• NO • Prostacyclin • Kinins
Circulating hormones	• Adrenaline • Nor adrenaline • Vasopressin • Angiotensin-II • Neuropeptide -Y	• Epinephrine in skeletal muscle & liver • Substance-P • Histamine • ANP • VIP

Regulation of blood pressure

- Blood pressure= cardiac output x peripheral resistance.

- S.I unit: PASCAL.
  - 1 mmHg= 0.133kPa.
  - 120/70 mmHg= 16/9.3kPa

- **Peripheral regulation [Baro receptors]**:
  - Stretch receptors in the walls of the heart and blood vessels.
  - They are the carotid sinus & Aortic bodies.

Receptor	Location	Afferent(Buffer nerves)	Centre	Efferent
Carotid sinus	• Small dilatation of the internal carotid artery above the bifurcation of common carotids	• Glossopharyngeal. N	• Medullary VMC[Vaso-Motor Centre (Nucleus Tractus Solitarius)]	• Sympathetic & • para sympathetic (Vagal)
Aortic bodies	• In the wall of arch of aorta	• Vagus.N		• Sympathetic & • para sympathetic (Vagal)

- ↑BP→Stimulation of baro receptors→ vagal stimulation + inhibition of VMC [↓ sympathetic activity]→ Vasodilatation, veno dilatation, ↓ BP, bradycardia, ↓ cardiac output.

Central regulation:
- Vasomotor centre→ group of neurons in the medulla that exerts a control over the blood pressure.

Afferents to VMC:
- Buffer nerves from carotid sinus & Aortic bodies.
- Increased blood pressure →buffer nerves→ nucleus tractus solitarius
- Tract 1: NTS→excitatory glutaminergic neurons → Caudal & intermediate ventrolateral medulla → stimulate GABA ergic neurons→ rostral ventro lateral medulla [RVLM]
- Tract 2: NTS → dorsal motor nucleus & Nucleus ambiguous →vagal neurons.

Direct stimulators of VMC	Excitatory inputs	Inhibitory inputs
CO_2, Hypoxia	• From cortex via hypothalamus • From pain pathways & muscles • From carotid & aortic chemo receptors	• From cortex via hypothalamus • From lungs • From carotid & aortic chemo receptors

Efferents from VMC:
- Sympathetic outflow: RVLM→ intermedio lateral gray column of spinal cord→ sympathetic preganglion.
- NT- glutamate.
- Stimulation =→ increased HR (Chrono tropic), Increased force of cardiac contraction(Ionotropic), vaso constriction, Increased BP, increased stroke volume & increased Cardiac output.
- Parasympathetic: dorsal motor nucleus & nucleus ambiguous→ vagus.
- Stimulation=→ vasodilatation, fall in BP, decreased HR & Cardiac output.

Note:
- chemoreceptor discharge may contribute to the production **of Mayer waves**- slow, regular oscilaations in the arterial pressure that occur st the rate of about one per 20-40 sec during hypotension. [**Traube-Hering waves**: fluctutaions in BP synchronous with respiration]

Effect of blood loss:

Blood loss	Blood pressure	Heart rate	Respiratory rate
• <15%	• No change	• Slight increase	• Normal
• 15-30%	• No change	• 100-120	• Increased
• 30-40%	• Reduced	• >120, weak	• >20
• >40%	• Markedly reduced	• >120, thready	• 20-30

Effect of gravity on blood pressure:

Positive 'g'	Negative 'g'
• occurs while ascending up • blood is rushed towards the lower limbs • cardiac output decreases • - black out of vision occurs	• occurs while diving • blood is rushed towards the head • cardiac output increases • - red out occurs

Factors that increase contractility(positive inotropism)

- **Increased heart rate**
  - When more action potentials occur per unit time
    - ✓ more Ca^{2+} enters the myocardial cells during the action potential plateaus
    - ✓ more Ca^{2+} is released from the **SR**
    - ✓ greater tension is produced during contraction.
    - ✓ Example of the affect of increased heart rate are:
- **Positive staircase,** or Bowditch staircase.
  - Increased heart rate
    - ✓ intracellular [Ca^{2+}] increases cumulatively over several beats.
    - ✓ increases the force of contraction in a stepwise fashion
- **Post-extrasystolic potentiation**
  - beat that occurs after an extrasystolic beat
  - because "extra" Ca^{2+} entered the cells during the extrasystole.
  - has **increased force of contraction**

Factors that increase contractility (positive inotropism)

- **Sympathetic stimulation (catecholamines) via β1 receptors**
- Increases the force of contraction by **two mechanisms:**
  - It increases **the inward Ca^{2+} current**
    - ✓ during the plateau of each cardiac action potential.
    - ✓ increases the activity of the Ca^{2+} pump of the SR by phosphorylation of **phospholamban**
    - ✓ as a result more Ca^{2+} is accumulated by SR
    - ✓ thus more Ca^{2+} is available for release in subsequent beats.
  - **Cardiac glycosides (digitalis) -Increase the force of contraction** by inhibiting Na^+, K^+ - ATPase in the myocardial cellmembrane
    - ✓ As a result of this inhibition intracellular [Na^+] increases
    - ✓ diminishing the Na^+ gradient across the cell membrane.
    - ✓ Na^+-Ca^{2+} exchange: a mechanism that extrudes Ca^{2+} from the cell
      - → depends on the size of the Na^+ gradient
      - → thus is diminished
      - → producing an increase in intracellular [Ca^{2+}].

Factors that decrease contractility (negative inotropism)

- **Parasympathetic stimulation (ACh) via muscarinic receptors**
- **during the plateau** of the cardiac action potential.
  - by decreasing the inward Ca^{2+} current
  - decreases the force of contraction in the **atria**

Length-tension relationship in the ventricles

- effect of ventricular muscle cell length on the force of contraction.
- similar to the relationship in skeletal muscle.

Preload

- is equivalent to **end-diastolic volume** related to **right atrial pressure.**
- When venous return increases
  - end-diastolic volume increases
  - stretches or lengthens the ventricular muscle fibers

Frank-Starling relationship

- **After load** for the left ventricle is equivalent to **aortic pressure**
  - Increases in aortic pressure **cause an increase in afterload on the left ventricle.**
  - for the right ventricle is equivalent to **pulmonary artery pressure**
  - Increases in pulmonary artery pressure
  - **cause increase in afterload on the right ventricle.**
- **Sarcomere length**
  - determines the maximum number of cross- bridges
  - that can form between actin and myosin.
  - determines the **maximum tension**, or **force of contraction.**

Velocity of contraction at a fixed muscle length

- maximal when the afterload is zero. decreased by **increases in afterload.**

- Frank-Starling relationship based on the **length-tension relationship** in ventricle
  - **Increases** in end-diastolic volume
    - ✓ cause an **increase** in ventricular fiber length
    - ✓ produces an **increase** in developed tension.
  - mechanism→**matches cardiac output to venous return**
    - ✓ greater the venous return=the greater the cardiac output.
  - Changes in contractility shift the Frank-Starling curve
  - ✓ upward (**increased contractility**) or
  - ✓ downward (**decreased contractility**).

Mean systemic pressure

- point at which the vascular function curve
- intersects the x-axis.
  - when there is "no flow" in the cardiovascular system-equals right atrial pressure
  - How is it measured when the heart is stopped experimentally
    - ✓ cardiac output and venous return are zero
    - ✓ pressure is equal throughout the cardiovascular system.

Regional circulation:

BLOOD FLOW TO VARIOUS ORGANS

	Rest (ml/min)	Exercise (ml/min)	Effect

CARDIAC OUTPUT	• 5900	• 24,000	• Increased
Blood Flow To:			
Skeletal muscle	• 650	• 20,850	• Increased
Heart	• 250	• 1000	• Increased
Brain	• 750	• 750	• **Unchanged**
Skin	• 500	• 500	• **Unchanged**
Inactive Skeletal muscle	• 650	• 300	• Decreased
Kidney, Liver, GIT etc	• 3100	• 600	• Decreased

Coronary circulation:

REGULATION OF CORONARY BLOOD FLOW			
Physical Factors	**Metabolic Factors**	**Neural Factors**	**Hormonal Factors**
• **Arterial BP:** • Diastolic BP. ↑es Coronary Blood flow more. • **Coronary Vascular resistances.** • **Extra – coronary vascular pressure.**	• Hypoxia**(Most Potent)** Hypercapnia • Acidosis	• **Sympathetics** • Vasodilatation(β - receptors) • Vasoconstriction(α - receptors)	• Vasopressin • Angiotensin • **Both of them ↓es Coronary** • **blood flow** • Thyroxine ↑ es Coronary blood flow

Peculiarities of Coronary Circulation:

- Heart is the only organ to generate its own perfusion pressure.
- Only organ in which the blood flow is decreased during Systole.
- Depends largely on anaerobic metabolism.
- Metabolic factors (hypoxia) are more potent regulators than neural factors.

Extra yields:

Atrial Natriuretic Peptide (ANP):

- Group of poly peptides produced by the atrial muscle cells.
- Stimulus: increased Nacl intake/ increase in ECF
- Effect: Diuresis & natriuresis by decreasing the effects of Aldosterone & ADH.

Bainbridge reflex:

- Rapid perfusion of blood or saline stimulates the **atrial receptors** & results in increased heart rate if the initial HR is low.

Bezold-Jarisch reflex:

- Serotonin & Chemicals like nicotine in the coronary or pulmonary arteries can stimulate the receptors of the left ventricle resulting in apnea, bradycardia & hypotension.

Triple response:

Red reaction	• Dilatation of pre capillary sphincters	• Release of histamine/bradykinin
Flare	• Dilatation of meta arterioles & pre capillary sphincters	• Mediated by branching of terminal axons of C fibres
Wheal	• Blister like appearance	• Increased capillary permeability

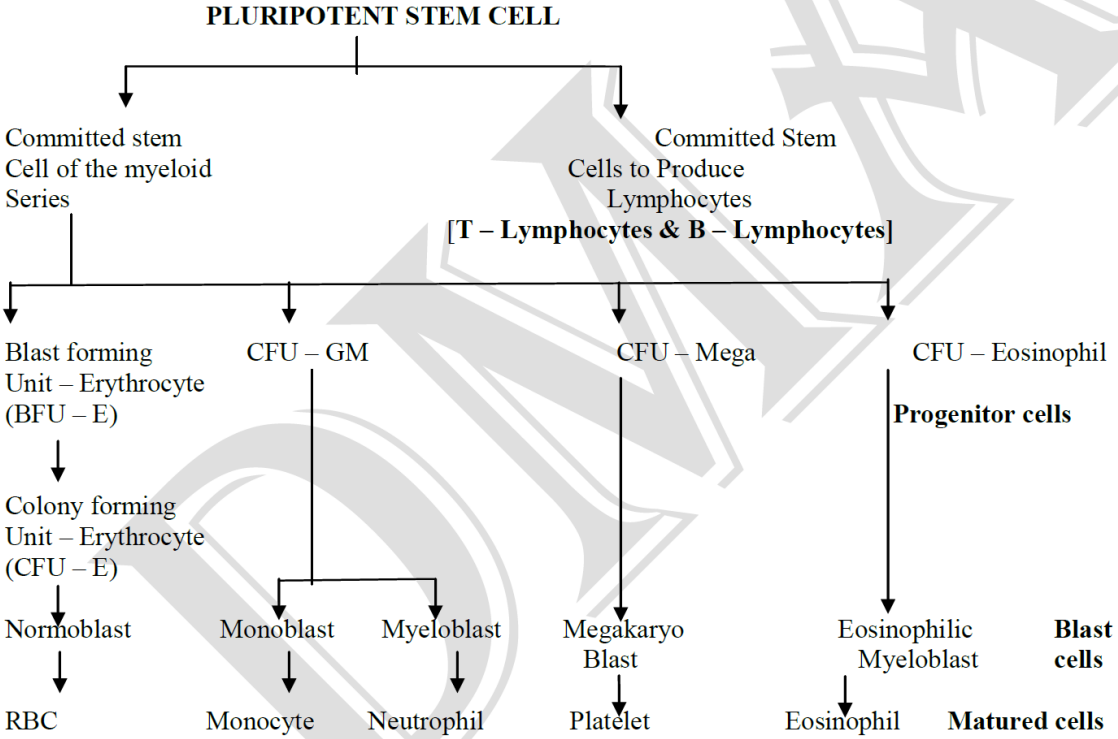
HEMATOLOGY

- Normal total Circulating Blood Volume: 5600ml (accounts for 8% of body weight)
- Normal Value = (70+10) ml/kg Body w

- **Plasma proteins**:
  - ✓ Albumin: (55%)
  - ✓ Globulin: (35%), 3 types [α, β, γ]
  - ✓ Fibrinogen & thrombin - 7%
- **Hemopoiesis:**

Fetus:	Adults:
• Ist trimester: Yolk sac • IInd trimester: Spleen & liver • IIIrd trimester: Mostly Bone Marrow	• up to 20yrs: All bones • After 20yrs: Flat bones

- After 20 years red BM gets converted into yellow BM in long bones.



- Hence, committed stem cells can form many cell types.

ABO Blood group systems:

- Type A individuals- A antigen +anti-B antibodies
- Type B individuals- B antigen+anti-A antibodies
- Type AB individuals- both A antigen & B antigen + **no antibodies**
- Type A individuals- **no antigen** + both anti-A antibodies & anti-B antibodies
- **Note:**
  - ✓ An **H gene** codes for a fucose transferase that adds a terminal fucose, forming the **H antigen** that is present in all blood types.
  - ✓ Type-A also expresses a second transferase that catalyses the placement of a terminal N-Acetylgalactosamine on the H antigen, whereas individuals who are type B express a transferase that places a terminal galactose.

- ✓ Individuals who are type AB have both transferases.
- ✓ Individuals who are type O have neither, so the H antigen persists.

AUTO IMMUNITY:

Organ specific or systemic auto-immunity:

- Type-1 DM (antibodies against pancreatic islet B cells)
- Myasthenia Gravis (antibodies against nicotinic cholinergic receptors)
- Multiple sclerosis (antibodies against myelin basic protein and other components of myelin)

Antibodies against receptors:

- Antibodies against TSH- Grave's disease.

Molecular mimicry:

- Production of antibodies against invading organisms that cross reacts with normal body constituents. Eg: Rheumatic fever following streptococcal infection.

Bystander effects:

- inflammation sensitizes the T cells of neighborhood.

Functions of RES or tissue Macrophage System

- Phagocytosis (Innate Immunity)
- Acquired immunity by i) Act as antigen presenting cells ii) Have receptors for complements & antibodies

Cytokines produced by macrophages

- i) IL-1 -activates T cells
- ii) IL-6 - activates lymphocytes
- Iii) IL-8 - chemo taxis
- iv) IL-12 - produce interferon 8
- v) TNM - promotes inflammation
- vi) GM-CSF - role in haemopoiesis.

RBC's:

- 62.5 % water, 35% hemoglobin
- Life span: 120 days.

ERYTHROPOIESIS:

- Hemocytoblast= stem cells
- Pro erythroblast= chromatins open
- Early normoblast= nucleoli disappears
- Intermediate normoblast = Hb starts appearing
- Late normoblast = nucleus degenerates, chromatin shows cart wheel appearance, mitosis stops.
- Reticulocyte: no nucleus.

Hemocytoblast➔ erythrocyte: 9 days.

- Normal bone marrow contains:
- 30%- Pro erythroblast & early normoblast
- 70%- Intermediate & late normoblast

Erythropoietin:

Source:

a. Kidneys: 85% by the interstitial cells in peri tubular capillary beds of kidney.
b. Liver: 15% by perivenous Hepatocytes.

Stimuli for secretion:

- Hypoxia (most potent)
- Alkalosis

- High altitude
- Androgens
- Catecholamines
- Adenosine

Regulation of Erythropoiesis

- 1% of RBC gets destroyed in 24 hrs.
- Complete turnover of RBC occurs once in 4 months.

Factors regulating erythropoiesis:

1. **Hypoxia – most potent stimuli**
2. **Nutrients**
   - Carbohydrates – for energy supply
   - Fat – for cell membrane synthesis
   - Proteins – for globin synthesis
   - Minerals – Iron – HEME synthesis
   - Copper – Hb biosynthesis
   - Vitamins – B12 & Folate – DNA synthesis
   - B6 – Cofactor in heme synthesis
   - Vit.C, Riboflavin, Pantothenate etc
   - Cobalt & Manganese
3. **Hormones**
   - Erythropoietin – Stimulates RBC Production
   - Thyroid Hormones – metabolism & maturation
   - Glucocorticoids – Stimulates Erythropoietin secretion
   - Androgens – Increases EPO secretion
   - **Oestrogen – Decreases EPO secretion**
   - Growth Hormone – Stimulate EPO Secretion
   - TSH, ACTH, Prolactin, cAMP, NAD, NADP,PG – E, PG – I, ADH, Nor-Adr, ,Serotonin, Angiotensin- Stimulates EPO Production

5. **Neural**
   - Stimulation of hypothalamus causes increased RBC Production (through ant pituitary or hypoxia)

Viscosity of blood

- 4-5 times more than water
- **Affected by:**
  - Hematocrit
  - Temperature
  - Flow Rate
  - Plasma Proteins
  - Diameter of a blood vessel.
- Viscosity is directly proportional to Hematocrit, concentration of plasma proteins & diameter of blood Vessels
- Viscosity is inversely proportional to temperature& flow rate.

Salient Points

- At high flow rates, i.e., at lower viscosities cells occupy the central axis of blood vessels while the cell – free zone of plasma moves parallel in the periphery. This is **plasma skimming.**
- As the Velocity decreases the viscosity increases and the RBC's stick to each other leading to **Rouleaux formation.**

LEUCOCYTES:

GRANULOCYTES:	AGRANULOCYTE:
• Neutrophils 60-70% • Eosinophils 1-4% • Basophils 0-1%	• Lymphocytes 25-30% • Monocytes 2-8%

Neutrophils:

- Life span- 6-30 hours. Half life- 6hrs
- **Arneth count**: counting the lobes of neutrophils.

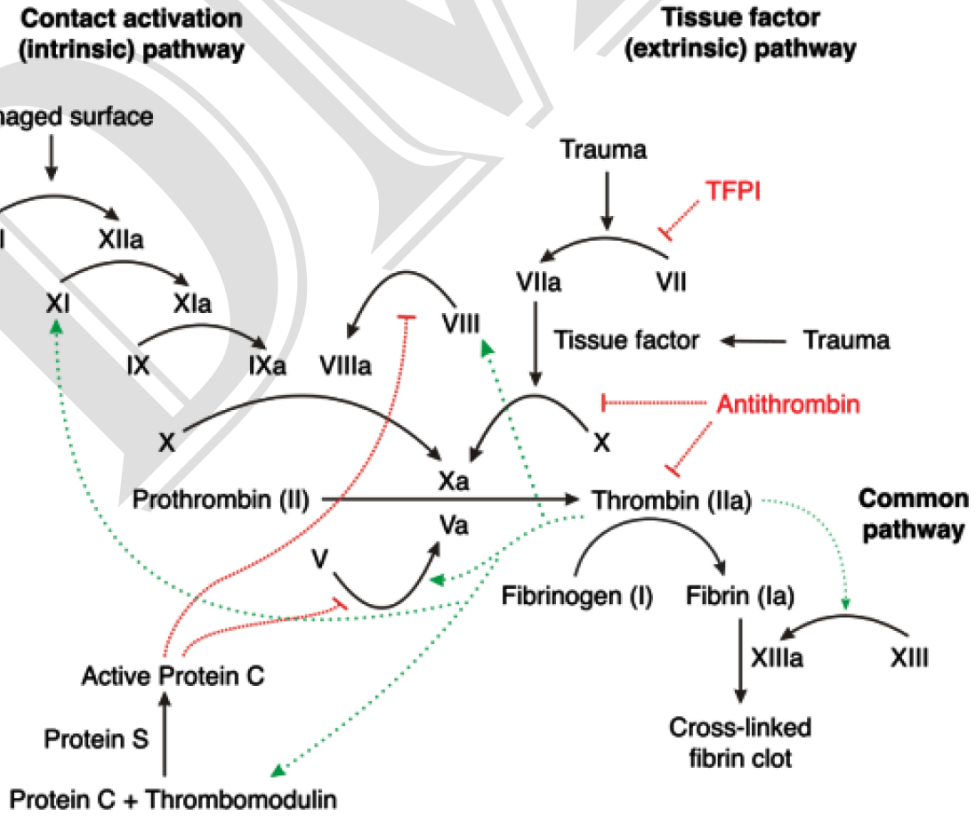
Granules of neutrophils:

Primary granules	Secondary granules
○ Appears at pro myelocytic stage	○ Appears at myelocytic stage
• **Contains:** ✓ Myeloperoxidase ✓ Hydroxylase ✓ lysosyme ✓ -Elastase ✓ -Cathepsin G ✓ -Defensin ✓ - Phospholipase A-2	• **Contains :** ✓ Lactoferrin ✓ lysosyme ✓ -alkaline phosphatase ✓ plasminogen activator ✓ - phospholipase A-2

Platelets:

- ○ Life span: 8-12 days
- ○ Platelet membrane contains receptors for:
  - Collagen
  - Fibrinogen
  - Von- Willebrand factor.
- ○ Cytoplasm contains:
  - Contractile proteins like thrombesthenin
  - Dense granules:
    - ○ Serotonin
    - ○ ADP
    - ○ ATP
  - α- granules:
  - clotting factors
  - PDGF

COAGULATION PATHWAYS



Leucocytosis(WBC count)	Leucopenia(WBC count)
○ **Physiological:** New born, high altitude, Exercise, after meals, High altitude ○ **Pathological:** • Fever(expect typhoid & viral fever) • Leukemias, Starvation, DM, uremia, Infections, pneumonia, MI	○ Aplastic anemia, Viral infection, TB, ○ Irradiation, Typhoid, Anti-metabolites ○ Megaloblastic anemia
Neutrophilia	**Neutropenia**
○ Pyogenic infection, Appendicitis, DM, Chemical Poisoning, MI, Malignancy	○ Aplastic Anemia, Irradiation, drug toxicity Typhoid & Viral infection
Eosinophilia	**Eosinopenia**
○ Asthma, Hay fever , Tropical eosinophilia , Allergy, Parasitic infestation	○ ACTH injection ○ Cushing's disease
Basophilia	**Basopenia**
○ Chronic Sinusitis, TB, Chicken pox, Hemolytic anemias	
Lymphocytosis	**Lymphocytopenia**
○ All Chronic diseases, TB, Syphilis, Infectious mononucleosis, Lymphocytic Leukemia, UTI ○ Diphtheria	○ TB, Irradiation, AIDS, ACTH treatment Cushing's Syndrome, Anti – metabolite treatment
Monocytosis	
○ Chronic diseases, Infectious mononucleosis, TB, Syphilis, monocytic leukemia, Hodgkin's disease, UTI, malaria, Carcinoma, Endocarditis, Protozoal infections	

Plasma expanders:

- Human albumin
- Dextran
- Hydroxy ethyl starch [Heta starch]
- Gelatin polymer
- Poly vinyl pyrrolidane

RESPIRATORY PHYSIOLOGY

- **Air passages:**
  - Between the trachea & alveolar sacs, the airways divide 23 times.

First 16 divisions	Terminal 7 divisions
• -Bronchi, bronchioles & terminal bronchioles • -intermediate bronchi-major airway resistance	• -Respiratory bronchioles, alveolar ducts & the alveoli **(Respiratory unit)**
• -mere conduction of air	• -respiratory zones of gaseous exchange.

- Alveoli lined by: two types of epithelial cells
  - Type-I cells: bulk of the alveoli
  - Type-II (CLARA) cells: secrete SURFACTANT.
- **Respiratory muscles:**
  - ✓ Inspiration- diaphragm, external intercostals.
  - ✓ Expiration-Passive process

BRONCHIAL TONE:

Broncho dilatation	Broncho constriction
• Inspiration • Sympathetic discharge • Evening • Epinephrine • VIP	• Expiration • Para- Sympathetic • Cholinergic discharge due stimulation of sensory receptors by irritants • Cool air, exercise, Cough • Early mornings • PAF, LT-B_4

LUNG VOLUMES & CAPACITIES

RESPIRATORY VOLUMES		
MEASUREMENT	**TYPICAL VALUE**	**DEFINITION**
Tidal volume(TV)	500ML	Amount of air that enters or leaves lungs during one inspiration or expiration (respiratory cycle).
Inspiratory reserve volume(IRV)	3000ML	Maximum extra volume of air that can be inspired over the normal TV
Expiratory reserve volume(ERV)	1200ML	Extra volume of air expired by forceful expiration after the end of normal tidal expiration
Residual volume(RV)	1200ML	amount of air left in lungs after forced exhalation
RESPIRATORY CAPACITIES		
MEASUREMENT	**TYPICAL VALUE**	**DEFINITION**
Vital capacity(VC)	4700ML	IRV+ TV + ERV, maximum amount of air that can be exhaled after a maximum inspiration
Inspiratory capacity(IC)	3500ML	TV + IRV, maximum amount of air that can be inhaled after a normal expiration
Functional residual capacity(FRC)	2400ML	RV+ERV, amount of air remaining in the lungs after a normal tidal expiration
Total lung capacity(TLC)	5900ML	RV+VC, maximum volume to which the lungs can be expanded

- Respiratory minute volume: 6L/min at rest
- Alveolar ventilation: 4.2L/min at rest
- Maximal voluntary ventilation: 125-170 L/min
- Work of quiet breathing-0.5kg-m/min
- Maximum Work of breathing-10kg-m/breath

- **Respiratory minute volume = tidal volume x respiratory rate**
- **Alveolar ventilation = [tidal volume- anatomical dead space] x respiratory rate**

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